

Substitute for Form 1449/A/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 1 of 15

Complete if Known

Application No.	09/939,208
Filing Date	08/24/2001
First Named Inventor	Gregory E. Agoston et al.
Group Art Unit	1616
Examiner Name	Qazi, S.
Attorney Docket Number	05213-0852 (43170-263550)

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No. ¹	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number ⁴	Kind Code ² (if known)			
	1	4,552,758		Murphy et al.	11/12/1985	
	2	4,808,402		Leibovich et al.	02/28/1989	
	3	5,629,340	A	Kuwano et al.	05/13/1997	
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	17	2002/0068724	A1	Slaga et al.	06/06/2002	

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FOREIGN PATENT DOCUMENTS									
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		Office ²	Number ⁴	Kind Code ³ (if known)					
	18	EPO	0166937	A2	Abbott Laboratories	08/01/1986			
	19	DE	27 57 157		Schering AG	12/19/1977			
	20	WO	93/19746	A1	ORION-YH-TYMA OY	10/14/1993			
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	25	Author: Title: Publ: Research Plus Catalog Vol/Iss: Pages: 50-58 Date: 1993			
	26	Author: Title: Registry Number: 56933-77-8 Publ: Chemical Abstracts Vol/Iss: Pages: Date:			
	27	Author: Title: Registry Number: 56933-78-9 Publ: Chemical Abstracts Vol/Iss: Pages: Date:			
	28	Author: Title: Registry Number: 57380-15-1 Publ: Chemical Abstracts Vol/Iss: Pages: Date:			
	29	Author: Title: Registry Number: 71782-94-0 Publ: Chemical Abstracts Vol/Iss: Pages: Date:			
	30	Author: Title: Registry Number: 71782-95-1 Publ: Chemical Abstracts Vol/Iss: Pages: Date:			
	31	Author: Title: Registry Number: 101277-11-6 Publ: Chemical Abstracts Vol/Iss: Pages: Date:			

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	32	Author: Title: Registry Number: 101429-40-7 Publ: <u>Chemical Abstracts</u> Vol/Iss: Pages: Date:			
	33	Author: Title: Registry Number: 162853-20-5 Publ: <u>Chemical Abstracts</u> Vol/Iss: Pages: Date:			
	34	Author: Title: News Article: Hoffman-La Roche Signs \$70 Million Deal with Millenium on Genomics Technology Publ: <u>Genetic Engineering News</u> Vol/Iss: Pages: Date: 4/15/1994			
	35	Author: Title: News Article: Advanced Drug Delivery Systems Peak Interest of Pharmaceutical & Biotech Firms Publ: <u>Genetic Engineering News</u> Vol/Iss: Pages: Date: 4/15/1994			
	36	Author: Title: News Article: Nasal Spray for Treating Bleeding Disorders Publ: <u>Genetic Engineering News</u> Vol/Iss: Pages: Date: 4/15/1994			
	37	Author: ALGIRE, G.H. et al. Title: Vascular reactions of normal and malignant tumors in vivo. I. Vascular reactions of mice to wounds and to normal and neoplastic transplants Publ: <u>Journal of the National Cancer Institute</u> Vol/Iss: 6 Pages: 73-85 Date: 08/1945			
	38	Author: ALIEV et al. Title: 54929q Synthesis of cycloalkyl derivatives of dihydric phenols and their ethers Publ: <u>Chemical Abstracts</u> Vol/Iss: 72 Pages: 370 Date: 1970			

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	39	Author: ANSTEAD et al. Title: The Estradiol Pharmacophore: Ligand Structure-Estrogen Receptor Binding Affinity Relationships and a Model for the Receptor Binding Site Publ: Steroids Vol/Iss: 62 Pages: 268-303 Date: 1997				
	40	Author: ATTALLA et al. Title: 2-Methoxyestradiol-Induced Phosphorylation of Bcl-2: Uncoupling from JNK/SAPK Activation (Abstract only) Publ: Biochemical and Biophysical Research Communications Vol/Iss: 247 (3) Pages: 616-619 Date: 6/29/1998				
	41	Author: BARNES et al. Title: Tumor Necrosis Factor Production in Patients with Leprosy Publ: Infection and Immunity Vol/Iss: 60 (4) Pages: 1441-1446 Date: 04/1992				
	42	Author: BINDRA et al. Title: Studies in Antifertility Agents. 8. Seco Steroids. 2. 5,6-Secoestradiol and Some Related Compounds Publ: Journal of Medicinal Chemistry Vol/Iss: 18 (9) Pages: 921-925 Date: 1975				
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	44	Author: BREM, H. et al. Title: Interstitial chemotherapy with drug polymer implants for the treatment of recurrent gliomas Publ: Journal of Neurosurgery Vol/Iss: 74 Pages: 441-446 Date: 03/01/91				
	45	Author: BURROWS, N.P. Title: Thalidomide Modifies Disease Publ: British Medical Journal Vol/Iss: 307 (6909) Pages: 939-940 Date: 10/09/93				

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	46	Author: CAMBIE et al. Title: Aromatic Steroids. Part I. Oxidation Products of 3-Methoxyestra-1,3,5(10)-triene- 17 β -yl Acetate Publ: J. Chem. Soc. Vol/Iss: Pages: 2603-2608 Date: 1968	
	47	Author: COREY et al. Title: Applications of N,N-Dimethylhydrazones to Synthesis. Use in Efficient, Positionally and Stereochemically Selective C-C Bond Formation; Oxidative Hydrolysis to Carbonyl Compounds Publ: Tetrahedron Letters Vol/Iss: 1 Pages: 3-6 Date: 1976	
	48	Author: COREY et al. Title: Facile Conversion of N,N-Dimethylhydrazones to Carbonyl Compounds by Cupric Ion-Catalyzed Hydrolysis Publ: Tetrahedron Letters Vol/Iss: 41 Pages: 36678-3668 Date: 1976	
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	50	Author: DING et al. Title: Sex Hormone-Binding Globulin Mediates Prostate Androgen Receptor Action via a Novel Signaling Pathway (Abstract only) Publ: Endocrinology Vol/Iss: 139 (1) Pages: 213-218 Date: 1998	
	51	Author: DURANI et al. Title: Seco-Oestradiols and Some Non-Steroidal Oestrogens: Structural Correlates of Oestrogenic Action Publ: Journal of Steroid Biochemistry Vol/Iss: 11 Pages: 67-77 Date: 1979	
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	53	Author: FEVIG et al. Title: A Short, Stereoselective Route to 16 α -(Substituted-alkyl)estradiol Derivatives Publ: <u>Journal of Organic Chemistry</u> Vol/Iss: 52 Pages: 247-251 Date: 1987			
	54	Author: FIELD et al. Title: Effect of Thalidomide on the Graft versus Host Reaction Publ: <u>Nature</u> Vol/Iss: 211 (5055) Pages: 1308-1310 Date: 09/17/66			
	55	Author: FIESER et al. Title: N-Methylformanilide Publ: <u>Organic Synthesis Collective Volume 3</u> Vol/Iss: 3 Pages: 590-591 Date: 1955			
	56	Author: FOLKMAN, J. Title: Tumor Angiogenesis: Therapeutic Implications Publ: <u>New England Journal of Medicine</u> Vol/Iss: 285 (21) Pages: 1182-1186 Date: 11/18/71			
	57	Author: FOLKMAN, J. et al. Title: Induction of Angiogenesis During the Transition from Hyperplasia to Neoplasia Publ: <u>Nature</u> Vol/Iss: 339 Pages: 58-61 Date: 05/04/89			
	58	Author: FOLKMAN, J. et al. Title: Tumor Behavior in Isolated Perfused Organs in vitro Growth and Metastases of Biopsy Material in Rabbit Thyroid and Canine Intestinal Segment Publ: <u>Annals of Surgery</u> Vol/Iss: 164(3) Pages: 491-502 Date: 09/01/66			
	59	Author: GADOSY et al. Title: Generation, Characterization, and Deprotonation of Phenol Radical Cations Publ: <u>Journal of Physical Chemistry</u> Vol/Iss: 103 Pages: 8834-8839 Date: 1999			

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	61	Author: GIMBRONE, M.A. et al. Title: Tumor Growth and Neovascularization: An Experimental Model Using the Rabbit Cornea Publ: Journal of the National Cancer Institute Vol/Iss: 52(2) Pages: 413-427 Date: 02/74			
	62	Author: GIMBRONE, M.A. et al. Title: Tumor dormancy <i>in vivo</i> by Prevention of Neovascularization Publ: Journal of Experimental Medicine Vol/Iss: 136 Pages: 261-276 Date: 1972			
	63	Author: GONZALEZ et al. Title: Synthesis and Pharmacological Evaluation of 8 α Estradiol Derivatives Publ: Steroids Vol/Iss: 40 (2) Pages: 171-187 Date: 9/1982			
	64	Author: GROSS, J.L. et al. Title: Modulation of Solid Tumor Growth <i>in vivo</i> by bFGF (Abstract only) Publ: Proceedings of the American Association of Cancer Research Vol/Iss: 31 Pages: 79 Date: 03/90			
	65	Author: GUNZLER, V. Title: Thalidomide-A Therapy for the Immunological Consequences of HIV Infection? Publ: Medical Hypothesis Vol/Iss: 30 (2) Pages: 105-109 Date: 10/89			
	66	Author: GUPTA et al. Title: Antifertility Agents. XIV. Secosteroids. VII. Synthesis of 2 α and 2 β , 6 β -dimethyl- 3 β -(p-hydroxyphenyl)-trans-bicyclo[4.3.0]nonan-7-ones and some related compounds (Abstract only) Publ: Indian Journal of Chemistry Vol/Iss: 13 (7) Pages: 759-760 Date: 1975			

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	67	Author: GUPTA et al. Title: Studies in Antifertility Agents. Part XVIII. 2 α -Diethyl-3 β -(p-hydroxyphenyl)-trans-bicyclo[4.3.0]nonan-7 β -ol and 6 β -methyl-3 β -(p-hydroxyphenyl)-2 α -propyl-trans-bicyclo[4.3.0]nonan-7 β -ol (Abstract only) Publ: Indian Journal of Chemistry Vol/Iss: 19B (10) Pages: 886-890 Date: 1980	
	68	Author: GUTIERREZ-RODRIGUEZ et al. Title: Treatment of Refractory Rheumatoid Arthritis - The Thalidomide Experience Publ: The Journal of Rheumatology Vol/Iss: 16 (2) Pages: 158-163 Date: 02/89	
	69	Author: GUTIERREZ-RODRIGUEZ, O. Title: Thalidomide - A Promising New Treatment for Rheumatoid Arthritis Publ: Arthritis and Rheumatism Vol/Iss: 27 (10) Pages: 1118-1121 Date: 10/84	
	70	Author: HAN et al. Title: Dehydroepiandrosterone and Dihydrotestosterone Recognition by Human Estrogenic 17 β -Hydroxysteroid Dehydrogenase Publ: Journal of Biological Chemistry Vol/Iss: 275 Iss 2 Pages: 1105-1111 Date: 1/14/2000	
	71	Author: HANDLEY et al. Title: Chronic bullous disease of childhood and ulcerative colitis Publ: British Journal of Dermatology Vol/Iss: 127 (40) Pages: 67-68 Date: 07/01/92	
	72	Author: HENEY et al. Title: Thalidomide treatment for chronic graft-versus-host disease Publ: British Journal of Haematology Vol/Iss: 78 (1) Pages: 23-27 Date: 05/91	
	73	Author: HORI, A. et al. Title: Suppression of Solid Tumor Growth by Immunoneutralizing Monoclonal Antibody Against Human Basic Fibroblasts Growth Factor Publ: Cancer Research Vol/Iss: 51 Pages: 6180-6184 Date: 11/15/91	

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	74	Author: IMAMURA et al. Title: Method for Manufacture of Dihydric Phenols (Abstract only) Publ: USPATFULL 76:20259 US 3,950,437 Vol/Iss: Pages: Date: 04/13/1976			
	75	Author: INGBER, D. et al. Title: Synthetic analogues of fumagillin that inhibit angiogenesis and suppress tumor growth Publ: Nature Vol/Iss: 348 Pages: 555-557 Date: 12/06/90			
	76	Author: JHINGRAN et al. Title: Studies in Antifertility Agents - Part XLI: Secosteroids-x: Syntheses of Various Stereoisomers of (+)-2,6β-diethyl-7α-ethynyl-3-(p-hydroxyphenyl)-trans-bicyclo [4.3.0]nonan-7β-ol. Publ: Steroids Vol/Iss: 42 (6) Pages: 627-634 Date: 1983			
	77	Author: KARWAT Title: Separation and Recovery of Hydrogen Sulfide from Hydrocarbon Mixture Publ: Caplus DE 1103310 Vol/Iss: Pages: Date: 09/02/1959			
	78	Author: KATAOKA et al. Title: An Agent that Increases Tumor Suppressor Transgene Product Coupled with Systemic Transgene Delivery Inhibits Growth of Metastatic Lung Cancer in Vivo (Abstract only) Publ: Cancer Research Vol/Iss: 58 (21) Pages: 4761-4765 Date: 11/1998			
	79	Author: KIM, K.J. et al. Title: Inhibition of Vascular Endothelial Growth Factor-induced Angiogenesis Suppresses Tumor Growth In Vivo Publ: Nature Vol/Iss: 362 Pages: 841-844 Date: 04/29/93			
	80	Author: KNIGHTON, D. et al. Title: Avascular and Vascular Phases of Tumour Growth in the Chick Embryo Publ: British Journal of Cancer Vol/Iss: 35 Pages: 347-356 Date: 1977			

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Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published			T*
	81	Author: KOLE et al. Title: Studies in Antifertility Agents. 11. Secosteroids. 5. Synthesis of 9,11-Secoestradiol Publ: Journal of Medicinal Chemistry Vol/Iss: 18 (7) Pages: 765-766 Date: 1975			
	82	Author: LEWIS, Richard J. Title: Publ: Hawley's Condensed Chemical Dictionary Vol/Iss: Pages: 577 Date: 01/1993			
	83	Author: LEWIS, Richard J. Title: Publ: Hawley's Condensed Chemical Dictionary Vol/Iss: Pages: 128-129 Date: 01/1993			
	84	Author: LIEN, W. et al. Title: The blood supply of experimental liver metastases. II. A Microcirculatory study of the normal and tumor vessels of the liver with the use of perfused silicone rubber Publ: Surgery Vol/Iss: 68 (2) Pages: 334-340 Date: 08/1970			
	85	Author: LIU et al. Title: Total Synthesis of (+)- $\Delta^{9(12)}$ -Capnellene Publ: Tetrahedron Letters Vol/Iss: 26 (40) Pages: 4847-4850 Date: 1985			
	86	Author: MARO et al. Title: Mechanism of Polar Body Formation in the Mouse Oocyte: An Interaction Between the Chromosomes, the Cytoskeleton and the Plasma Membrane Publ: Journal of Embryology and Experimental Morphology Vol/Iss: 92 Pages: 11-32 Date: 1986			
	87	Author: MEZA et al. Title: Managing the Gastrointestinal Complications of AIDS Publ: Drug Therapy Vol/Iss: 23 (11) Pages: 74-83 Date: 11/1993			

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¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

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Substitute for Form 1449/A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Complete if Known	
				Application No.	09/939,208
				Filing Date	08/24/2001
				First Named Inventor	Gregory E. Agoston et al.
				Group Art Unit	1616
				Examiner Name	Qazi, S.
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	88	Author: NAAFS et al. Title: Thalidomide Therapy An Open Trial Publ: International Journal of Dermatology Vol/Iss: 24 (2) Pages: 131-134 Date: 03/1985			
	89	Author: NAMBARA et al. Title: Synthesis of 16 β -Oxygenated Catechol Estrogen Methyl Ethers, New and Potential Metabolites Publ: Chemical & Pharmaceutical Bulletin Vol/Iss: 23 (7) Pages: 1613-1616 Date: 07/1975			
	90	Author: NEWKOME et al. Title: Synthesis of Simple Hydrazones of Carbonyl Compounds by an Exchange Reaction Publ: Journal of Organic Chemistry Vol/Iss: 31 Pages: 677-681 Date: 03/1966			
	91	Author: NGUYEN, M. et al. Title: Elevated Levels of the Angiogenic Peptide Basic Fibroblast Growth Factor in Urine of Bladder Cancer Patients Publ: Journal of the National Cancer Institute Vol/Iss: 85 (3) Pages: 241-242 Date: 02/03/93			
	92	Author: PAKALA et al. Title: Modulation of Endothelial Cell Proliferation by Retinoid x Receptor Agonists Publ: European Journal of Pharmacology Vol/Iss: 385 (2/3) Pages: 255-261 Date: 09/1999			
	93	Author: PENG et al. Title: Synthesis and Optical Properties of Novel Unsymmetrical Conjugated Dendrimers Publ: Journal of the American Chemical Society Vol/Iss: 122 Pages: 6619-6623 Date: 2000			
	94	Author: POWELL et al. Title: Investigation and Treatment of Orogenital Ulceration; studies on a Possible Mode of Action of Thalidomide Publ: British Journal of Dermatology Vol/Iss: 113 Supp. 28 Pages: 141-144 Date: 07/1985			

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	95	Author: ROMANELLI et al. Title: Ethyl-p-Dimethylaminophenylacetate Publ: Organic Synthesis Vol/Iss: 5 Pages: 552 Date:				
	96	Author: SEEGERs et al. Title: The Mammalian Metabolite, 2-methoxyestradiol, Affects P53 Levels and Apoptosis Induction in Transformed Cells but Not in Normal Cells (Abstract only) Publ: Journal of Steroid Biochemistry and Molecular Biology Vol/Iss: 62 (4) Pages: 253-267 Date: 07/1997				
	97	Author: SHAH et al. Title: (+/-)-(N-alkylamino)benzazepine Analogs: Novel Dopamine D1 Receptor Antagonists Publ: Journal of Medicinal Chemistry Vol/Iss: 38 (21) Pages: 4284-4293 Date: 10/13/95				
	98	Author: SIDKY et al. Title: Inhibition of Angiogenesis by Interferons: Effects on Tumor- and Lymphocyte-induced Vascular Responses Publ: Cancer Research Vol/Iss: 47 Pages: 5155-5161 Date: 10/01/87				
	99	Author: SRIVASTAVA, A. et al. Title: The Prognostic Significance of Tumor Vascularity in Intermediate-Thickness (0.76-4.0 mm Thick) Skin Melanoma Publ: American Journal of Pathology Vol/Iss: 133 (2) Pages: 419-424 Date: 11/1988				
	100	Author: STARKOV et al. Title: Mono- and Dialkylolation of Guaiacol by Olefins on KU-2 Cation Exchanger (Abstract only) Publ: Zhurnal Prikladnoi Khimii Vol/Iss: 41 (3) Pages: 688-690 Date: 1968				
	101	Author: TAYLOR, S. et al. Title: Protamine is an Inhibitor of Angiogenesis Publ: Nature Vol/Iss: 297 Pages: 307-312 Date: 05/27/82				

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	102	Author: TREMBLAY et al. Title: A Convenient Synthetic Method for Alpha-Alkylation of Steroidal 17-Ketone: Preparation of 16 β -(THPO-Heptyl)-Estradiol Publ: <u>Synthetic Communications</u> Vol/Iss: 25 (16) Pages: 2483-2495 Date: 1995				
	103	Author: TREMBLAY et al. Title: Synthesis of 16-(Bromoalkyl)-Estradiols Having Inhibitory Effect on Human Placental Estradiol 17 β -Hydroxysteroid Dehydrogenase (17 β HSD Type 1) Publ: <u>Bioorganic & Medicinal Chemistry</u> Vol/Iss: 3 (5) Pages: 505-523 Date: 1995				
	104	Author: VICENTE et al. Title: In Vitro Activity of Thalidomide Against Mycobacterium avium Complex Publ: <u>Archives of Internal Medicine</u> Vol/Iss: 153 (4) Pages: 534 Date: 02/22/93				
	105	Author: WEIDNER, N. et al. Title: Tumor angiogenesis: A New Significant and Independent Prognostic Indicator in Early-Stage Breast Carcinoma Publ: <u>Journal of the National Cancer Institute</u> Vol/Iss: 84 Pages: 1875-1887 Date: 12/16/92				
	106	Author: WEIDNER, N. et al. Title: Tumor Angiogenesis Correlates with Metastasis in Invasive Prostate Carcinoma Publ: <u>American Journal of Pathology</u> Vol/Iss: 143 (2) Pages: 401-409 Date: 08/1993				
	107	Author: WEIDNER, N. et al. Title: Tumor Angiogenesis and Metastasis-Correlation in Invasive Breast Carcinoma Publ: <u>New England Journal of Medicine</u> Vol/Iss: 324 (1) Pages: 1-8 Date: 01/03/91				
	108	Author: WELSCH et al. Title: Staphylostatic Activity of Some New Diphenols, Naphthols, and Chalcones (Abstract only) Publ: <u>Experientia</u> Vol/Iss: 11 Pages: 350-351 Date: 1955				

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	109	Author: WHITE et al. Title: Treatment of Pulmonary Hemangiomas with Recombinant Interferon Alfa-2a Publ: The New England Journal of Medicine Vol/Iss: 32 (18) Pages: 1197-1200 Date: 05/04/89			
	110	Author: ZOUBINE et al. Title: 2-Methoxyestradiol-Induced Growth Suppression and Lethality in Estrogen-Responsive MCF-7 Cells May Be Mediated by Down Regulation of p34cdc2 and Cyclin B1 Expression (Abstract only) Publ: International Journal of Oncology Vol/Iss: 15 (4) Pages: 639-646 Date: 10/1999			

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